Remarks

Introduction

Claims 1-11 were pending. By way of this response, the specification has been amended to correct various inadvertent grammatical and typographical errors, and claims 1, 6, and 11 have been amended, claim 7 has been cancelled without prejudice. Support for the amendments to the specification and the claims can be found in the application as originally filed, and no new matter has been added. Accordingly, claims 1-6 and 8-11 are currently pending.

Information Disclosure Statement

The Office Action indicates that the Information Disclosure Statement refers to an improperly cited document (U.S. App. No. 10/194,805) and that the crossed-out articles were not present.

Applicant disagrees that U.S. App. No. 10/194,805 is improperly cited. The application was submitted in accordance with 37 CFR §§ 1.97(a)(1) and 1.98(b)(3). Therefore, applicant requests that U.S. App. No. 10/194,805 be considered by the Examiner and an initialed Form-1449 be returned to applicant. Applicant will be resubmitting the crossed-out articles that were originally submitted and allegedly not present for the Examiner.

Specification

The specification has been objected for various formalities.

Applicant submits that the amendments to the specification as set forth above address the objection. Therefore, applicant submits the objection has been overcome and requests the objection be withdrawn.

Claim Objections

Claim 7 has been objected to because the word "from" was misspelled.

Claim 7 has been cancelled, as set forth above. Therefore, applicant submits the objection is moot.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1-11 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled. In short, the rejection is based on the specification's lack of working examples. In addition, claims 1-3, 5, and 11 have been rejected because they recite the administration of any amount of any botulinum toxin to a patient.

Claims 1 and 11 have been amended to indicate that the amount of botulinum toxin administered to the patient is a therapeutically effective amount. Thus, the present claims recite amounts of botulinum toxin which are not lethal.

Applicant traverses the rejection as it relates to the present claims.

The Office Action implies that the lack of working examples in the specification indicates that the present claims are not

enabled by the specification under 35 U.S.C. § 112, first paragraph. Applicant submits that working examples are not required to be provided in an application in order to comply with 35 U.S.C. § 112. It is well established caselaw that a specification need not contain working examples if, coupled with information known in the art, the invention is otherwise disclosed in the specification in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation (In re Borkowski and Van Venrooy, 164 USPQ 642 (CCPA 1970)).

At least in view of the disclosure of Examples 1 to 4, and the detailed description in general, one skilled in the art would have been able to practice the claimed methods without an undue amount of experimentation. Note that the specification clearly states how to make and how to use the invention. For example, the specification indicates that botulinum toxin is commercially available from companies, including Allergan (page 3 and page 10 of the specification). The specification indicates how to use the botulinum toxin to treat a skin disorder, including warts, corns, calluses, and bunions, by topically, subdermally, or intradermally administering the botulinum toxin to a patient having a skin disorder (page 20, lines 2-10). In addition, the specification indicates how to determine the therapeutic efficacy of the administration of the botulinum toxin (e.g., the efficacy of the botulinum toxin in treating the skin disorder; see page 36, lines 5-18; Examples 1-4; and page 39, line 17 to page 40, line 3).

Thus, applicant submits that a physician with ordinary skill in the art would be able, without an undue amount of experimentation, to use applicant's teaching to obtain a desired

amount of a botulinum toxin, such as a therapeutically effective amount of botulinum toxin, identify a skin disorder, such as a wart, corn, callus, neuroma, ulcer, hammertoe and bunion, administer the botulinum toxin to the patient, and evaluate whether the administration was therapeutically effective. This method or approach is routine testing to persons skilled in the art (e.g., see page 30, lines 18-27; page 35, line 22 to page 36, line 3) and does not involve undue experimentation.

In the present case, applicant has disclosed, by example, therapeutic efficacy of botulinum toxin types A-G in treating various skin disorders, including those recited in the present claims. Furthermore, applicant has disclosed how to administer the neurotoxin, where to administer the neurotoxin, and appropriate formulations for the neurotoxin. Following the instructions provided by applicant it is a simple and routine matter for one skilled in the art to use a botulinum toxin to treat a skin disorder that comprises warts, corns, calluses, neuromas, ulcers, hammertoe or bunions, as recited in the present claims.

As acknowledged by the Examiner, the determination of undue experimentation involves a balancing of the factors enumerated in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988) citing In re Forman (In re Forman, 230 USPQ 546 (Bd.Pat.App. & Int.1986)). These factors include: a) the quantity of experimentation necessary; b) the amount of guidance presented; c) the presence or absence of working examples; d) the nature of the invention; e) the state of the prior art; f) the relative skill of those in the art; g) the predictability or unpredictability of the art; and h) the breadth of the claims.

Applicant respectfully submits that the "Forman factors" have been met by applicant's disclosure, for the reasons set forth herein:

A. THE QUANTITY OF EXPERIMENTATION NECESSARY

Applicant's use of well known administration methods and neurotoxins, provide sufficient guidance for a skilled artisan to evaluate the efficacy of botulinum toxin, let alone any neurotoxin, in the claimed method. Given the teachings of the instant application, one skilled in the art would readily be able to obtain a suitable composition containing a botulinum toxin, would be able to determine an administration site for the toxin, administer the toxin, and determine whether the administration was effective. Accordingly, the specification provides the requisite guidelines to practice the invention without undue experimentation. While some additional effort may be required to optimize the claimed methods in the context of determining the optimal dosage or therapeutic schedule for treating skin disorders, such refinements would be provided during clinical trials and are not required for enablement of the claimed invention.

B. THE AMOUNT OF DIRECTION OR GUIDANCE PRESENTED

The disclosure of the instant application, as a whole, discloses that different serotypes of botulinum toxin may be used to treat patients with skin disorders. In addition, the instant application discloses how to make and use botulinum toxins to practice the invention, how to prepare a suitable composition containing botulinum toxin; how and where to administer the botulinum toxin; and amounts of different

botulinum toxins used to treat skin disorders, as indicated above. Examples 1-4 provide disclosure of the use of one botulinum toxin serotype. The examples simply provide more detail to complement the rest of the disclosure of the invention. Thus, given the disclosure of the entire specification, physicians skilled in the art can readily determine how to make and use the present invention. Any additional adjustments that may be needed, such as adjusting dosages, would simply be to optimize the therapeutic effects of the treatment, and clearly, such optimization would be routine to persons of ordinary skill in the art, and are not necessary to enable an invention.

Indeed, the courts have held that determining proper dosage amounts for an established treatment is routine and could be adjusted to suit the needs of an individual (U.S. v. Telectronics, Inc., 8 USPQ2d 1217, 1223 (Fed. Cir. 1988)). In addition, the specification specifically states that the "the appropriate route of administration and dosage are generally determined on a case by case basis by the attending physician. Such determinations are routine to one of ordinary skill in the art (see for example, *Harrison's Principles of Internal Medicine* (1998) ..." (page 30, lines 19-22). Although other factors may need to be considered in optimizing the treatment protocol before actual clinical use, such factors do not require consideration to satisfy enablement under 35 U.S.C. § 112, and are not requirements for patentability. Therefore, applicant respectfully contends that the specification is enabling because those skilled in the art would know how to conduct a dose response study and perform other procedures as needed to determine the appropriate amounts of botulinum toxin to be used to treat a skin disorder without undue experimentation.

C. THE PRESENCE OR ABSENCE OF WORKING EXAMPLES

Working examples are not required to enable an invention, as noted above. In the present case applicant has disclosed, by specific example, how to locate an area to be administered with a neurotoxin; how to administer the neurotoxin to the patient with a skin disorder; and how to evaluate the effectiveness of the treatment (e.g., page 37, line 1 to page 39, line 11). Following the instructions provided by applicant, it would have been a simple and routine matter for one skilled in the art to use a neurotoxin, such as botulinum toxin, to treat skin disorders of patients.

D. THE NATURE OF THE INVENTION

The invention relates to a method of treating skin disorders of patients by administering botulinum toxin to the patients. The present invention recites that the skin disorders include specific conditions, such as warts, corns, calluses, neuromas, ulcers, hammertoes and bunions. The underlying requirement is that botulinum toxin is administered to a patient to treat at least one of the specified skin disorders. The methods of administering botulinum toxin were well known to those skilled in the art. In addition, the compositions containing botulinum toxin are relatively simple. For example, an injectable composition may contain botulinum toxin, a tonicity adjustment agent, such as sodium chloride, and a stabilizer, such as human serum albumin. The composition can either be in liquid or lyophilized forms. Or, the composition may include a botulinum toxin associated with a polymeric component in the form of an implant. Or the composition may

include a botulinum toxin with excipients useful for topical application. The particular embodiments of the invention involving a type A botulinum toxin, are, to be considered as illustrative and not restrictive.

It remains uncontroverted that similar methods involving botulinum toxins are enabled. Indeed, the use of botulinum toxin to treat skin lesions is the subject matter of U.S. Pat. No. 5,670,484.

E. THE STATE OF THE PRIOR ART

Information about the state of the art that is relevant to the analysis of whether undue experimentation would have been required concerns, whether those skilled in the art are sufficiently familiar with the methods needed to practice the invention . As discussed herein, applicant's methods of administering botulinum toxins known in the art (e.g., see some administration methods disclosed in U.S. Pat. No. 5,670,484) were sufficiently well known at the time of the invention to reduce the amount of experimentation required to practice the claimed methods. For example, as disclosed in the instant specification, botulinum toxin type A has been administered to patients to treat blepharospasm, cervical dystonia, oromandibular dystonia, and spasmodic dysphonia. However, the art was silent as to whether botulinum toxins could effectively treat skin disorders such as warts, corns, calluses, neuromas, ulcers, hammertoes and bunions.

F. THE RELATIVE SKILL OF THOSE IN THE ART

There was a high level of skill in the art at the time of applicant's invention . Physicians having medical degrees and years of residential training and experience are the norm. It was well within the skill of those in art to practice the claimed invention in view of applicant's disclosure and what was known in the art. For example, the methods disclosed by the above-identified application teach how to prepare pharmaceutical compositions containing botulinum toxin and how to administer the toxins to treat skin disorders.

Additionally, at the time of the present invention, numerous publications were available that taught physiological and biochemical properties of botulinum toxins, and that taught how to administer botulinum toxin to muscles and skin. In addition, publications have described therapeutic effects mediated by botulinum toxins.

Since the skill in the art was quite high, it would not have required undue experimentation on the part of the skilled artisan, given the disclosure of the above-identified application, to administer a botulinum toxin to a patient to treat one or more skin disorders of that patient. Thus, at the time of the present invention, all of the ingredients were available to practice the present invention with a variety of botulinum toxins.

G. THE PREDICTABILITY OR UNPREDICTABILITY OF THE ART

While there will always be some unpredictability in introducing an agent into the human body, such unpredictability

would not involve undue experimentation in view of the disclosure of the relevant methods disclosed in the instant application. Just because botulinum toxins are highly toxic agents does not mean that the use of botulinum toxins would be so unpredictable that the use would require an undue amount of experimentation. As discussed herein, the instant application provides sufficient teaching and guidance to enable one skilled in the art to practice the invention without an undue amount of experimentation.

H. THE BREADTH OF THE CLAIMS

Applicant's claims are tailored to methods for treating skin disorders which include warts, corns, calluses, neuromas, ulcers, hammertoes and bunions. The breadth of the claims is commensurate with the disclosure of the application, which describes how to make and use botulinum toxin to treat skin disorders in general, and the conditions specifically recited in the claims in particular.

Thus, because the specification of the instant application describes the claimed invention in such a manner that one of ordinary skill in the art can practice the invention, and because the specification, including the examples, disclose that botulinum toxin may be effectively used to treat skin disorders, applicant respectfully requests the Examiner to withdraw the rejections.

In view of the above, applicant submits that present claims satisfy the requirements of 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. § 102

Claims 1-6, 7, and 9 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Binder (U.S. Pat. No. 5,670,484). Claims 1-6 and 10 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Binder (EP 0845267).

Applicant notes that U.S. Patent No. 5,670,484 and EP 0845267 are substantially identical in disclosure. Therefore, the references will be referred to herein collectively as "Binder".

In addition, applicant notes that claims 7 and 11 were not rejected over EP 0845267. Applicant submits that at least for this reason, claim 7 should not be rejected over U.S. Patent No. 5,670,484 because neither of these references disclose, teach, or even suggest a skin disorder such as warts, corns, calluses, neuromas, ulcers, hammertoes and bunions, as recited in the present claims.

Independent claims 1, 6, and 10 have been amended as set forth above. Applicant traverses the rejections as they relate to the present claims.

Applicant submits that Binder does not disclose, teach, or suggest the present invention. For example, Binder does not disclose, teach, or even suggest a skin disorder such as warts, corns, calluses, neuromas, ulcers, hammertoes and bunions, as recited in the present claims. Indeed, this is supported by the Examiner's lack of rejection of claim 11 over U.S. Pat. No.

5,670,484 and lack of rejection of claim 7 and 11 over EP 0845267.

Binder discloses administration of a botulinum toxin to treat skin lesions associated with cutaneous cell-proliferative disorders. Based on a computerized text search, Binder does not even contain any of the words: warts, corns, calluses, neuromas, ulcers, hammertoes and bunions.

The present claims recite that the skin disorder treated by administration of a botulinum toxin comprises a disorder selected from the group consisting of warts, corns, calluses, neuromas, ulcers, hammertoes and bunions (i.e., claims 1 and 6) or the disorder is warts (claim 11).

Because Binder does not disclose or teach each and every limitation recited in the present claims, applicant submits that the present claims are not anticipated by Binder.

In addition, applicant submits that Binder does not suggest the present invention. For example, Binder discloses that the conditions being treated are psoriasis, dermatitis, eczema, and pyriatis rosea. These conditions are caused by excessive cell proliferation.

Binder does not disclose, teach, or even suggest treatment of a skin disorder comprising warts, corns, calluses, neuromas, ulcers, hammertoes or bunions. As stated above, the conditions disclosed by Binder are conditions associated with cell-proliferation. The specific conditions recited in the present claims and cell-proliferation disorders are different and distinct, one from the other. For example, as described in the

specification, a bunion can be understood to be a localized swelling that may be caused by an inflamed bursa, a callus, including a corn, may be a thickened layer of skin formed by repeated rubbing of the skin at a certain location, a hammertoe condition may be an abnormal contraction or buckling of the toe, which may be involved in formation of a callus, an ulcer may be a slow healing skin wound, warts may be skin growths caused by a papillomavirus, and a neuroma may be a swelling or scarring of a small nerve that connects to toes. The specific conditions recited in the present claims, and identified above, may be understood to be attributed to causes other than cell-proliferation. Thus, applicant submits that Binder's disclosure of cell proliferative disorders does not even suggest disorders which include warts, corns, calluses, neuromas, ulcers, hammertoes or bunions.

In view of the above, applicant submits that the present claims, that is claims 1-6 and 8-11, are not anticipated by, and are unobvious from and patentable over Binder (i.e., U.S. Pat. No. 5,670,484 and EP 0845267) under 35 U.S.C. §§ 102 and 103.

In addition, each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present methods including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

Conclusion

In conclusion, applicant has shown that the present specification is in proper form, that the present claims satisfy the requirements of 35 U.S.C. § 112, and are not anticipated by and are unobvious from and patentable over the prior art under 35 U.S.C. §§ 102 and 103. Therefore, applicant submits that the present claims, that is claims 1-6 and 8-11 are allowable. Therefore, applicant respectfully requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Respectfully submitted,

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